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### **The Impact of the Use of Menthol in Cigarettes on the Public Health**

Legacy submits these comments to the Tobacco Product Scientific Advisory Committee (TPSAC) in support of our view that a careful and fair review of the scientific evidence demonstrates that the issuance of a tobacco product standard banning the use of menthol in cigarettes as a characterizing flavor would be “appropriate for the protection of the public health” as set out in the Family Smoking Prevention and Tobacco Control Act (Tobacco Control Act).

As discussed in more detail below, after reviewing and evaluating the scientific evidence, we have concluded that it is more likely than not that:

- Menthol flavoring is associated with both youth smoking initiation and decreased smoking cessation; and
- Prohibiting menthol as a cigarette flavoring would result in (a) reduced smoking initiation; (b) increased smoking cessation; and (c) a reduction in the number of Americans who die or are harmed from tobacco products.

We hope that these comments will assist TPSAC in its review of the evidence in accordance with the statute and in formulating its recommendations to the FDA.

### **The Statutory Framework**

This submission focuses on a review of the scientific evidence in keeping with TPSAC’s mission and expertise. However, it is important to keep in mind the statutory framework governing the consideration of a menthol ban, even as part of the review of the science, since the science must be evaluated in a manner consistent with the applicable legal standards. The Tobacco Control Act authorizes the Secretary to issue tobacco product standards, including a ban on menthol, that are appropriate for the protection of the public health. Recognizing the need for a new standard to govern the regulation of tobacco, since the traditional safe and effective standard is plainly inappropriate in this context, Congress designed the new “public health standard . . . to be a flexible standard that focuses on the overall goal of reducing the number of individuals who die or are harmed by tobacco products.”<sup>1</sup>

More specifically, the standard calls for the review of the scientific evidence regarding (1) the risks and benefits of the tobacco product standard to the population as a whole, including both users and non-users of tobacco products; (2) whether there is an increased or decreased likelihood that existing users of tobacco products will stop using such

products and (3) whether there is an increased or decreased likelihood that those who do not currently use tobacco products, most notably youth, will start to use tobacco products.<sup>2</sup>

Importantly, the Tobacco Control Act does not impose a causation standard and TPSAC should resist entreaties to analyze the scientific evidence through the prism of causation. Rather, Congress carefully framed the controlling standard in terms of risks, benefits and likelihoods. Congress recognized that, in order to stem the tide of the tobacco epidemic, it is absolutely critical to stop new—overwhelmingly young—smokers from starting and to help established smokers to quit.<sup>3</sup> In addition, Congress was particularly concerned with a tobacco product standard’s likely impact on initiation and cessation rates and not just with its impact on the health of current smokers.<sup>2</sup>

### **Standards for Evidence Review and Classification**

Consistent with the Tobacco Control Act’s standards, we did *not* attempt to establish that menthol flavoring *causes* either youth smoking initiation or decreased smoking cessation. Rather, we examined the evidence to assess relationships between menthol cigarette use, youth initiation, and adult cessation and to determine whether there was a *likelihood* that prohibiting menthol would reduce the number of smokers and thereby provide benefit to our nation’s public health. This approach is consistent with the recommendations for evidence review and classification presented at the October 7, 2010 TPSAC meeting. Accordingly, our review of the scientific evidence related to the risks, benefits and likely results of an FDA ban on menthol flavoring in cigarettes follows these recommendations. First, with regard to the sources of evidence, we have undertaken a review of the peer-reviewed literature. We also address certain additional scientific evidence that has been developed. While we provide context for some of our findings with tobacco industry and related documents, we did not complete a comprehensive search of the publicly available tobacco documents. We strongly encourage FDA to undertake or commission such a review and also to obtain all menthol-related studies and data from the tobacco companies pursuant to its authority under the Tobacco Control Act.

Second, in reviewing the scientific literature, we have been guided by broadly accepted standards of evidence synthesis. In reviewing and evaluating available published epidemiologic studies on tobacco use among adults and youth, we:

- (1) Examined the methods and designs of the studies, the rigor with which they were conducted, and the limits of interpreting data with respect to the population, place, and time of the study;
- (2) Categorized individual studies according to their methods and design and evaluated studies that used comparable methods to determine consistency of the evidence across populations and over time. We examined evidence across these comparable studies to assess the strength of the association and to determine if a temporal relationship was present between menthol cigarette use and smoking initiation or cessation;
- (3) Looked at the body of scientific evidence to determine whether findings of individual studies were coherent with each other and with our broader understanding of tobacco use in the United States; and

- (4) Considered the plausibility of these findings in the context of tobacco industry and related documents.

Third, we asked whether positive relationships<sup>i</sup> exist and whether chance, bias, and confounding could be ruled out with reasonable confidence. In keeping with a classification scheme based on the concept of equipoise, and recognizing that decision-makers must often act in the face of scientific uncertainty, we asked whether:

- The evidence is sufficient to conclude that a relationship is more likely than not;
- The evidence shows that a relationship is at least as likely as not;
- The evidence is insufficient to conclude that a relationship is more likely than not; or
- There is insufficient evidence to make a determination of strength of evidence.

The second category—evidence suggestive but not dispositive of a relationship—would come into play, for example, in the presence of some inconsistency in study results or studies where chance, bias and confounding could not be ruled out with confidence. Mindful of the fact that the Tobacco Control Act standard is framed in terms of risks, benefits and likelihoods, and not certainty or causality, we believe that evidence that shows that a relationship is at least as likely as not would adequately support the required statutory findings. Nonetheless, as we discuss below, the scientific evidence regarding the relationship between menthol and both initiation and cessation is sufficient to conclude that relationships are more likely than not.

Finally, consistent with the statutory framework, our review focused on the likely impact of a menthol ban on a broad population-wide basis, rather than on a more narrow impact on current menthol users at the individual level. In addition, in considering the strength of the evidence, we stayed mindful of the public health purposes of the Tobacco Control Act and the precept that it should be broadly construed to achieve its remedial purposes.<sup>4</sup>

A listing and brief descriptions of the studies from which the results and conclusions are drawn are included in the Appendix to these comments.

### **The Scientific Evidence on Menthol and Youth Smoking Demonstrates a Likelihood That a Ban on Menthol Will Result in Lower Rates of Youth Smoking Initiation**

The predicate facts are clear: young smokers and, even more so new young smokers, smoke menthol cigarettes at rates that are significantly higher than the rates at which young adults and adults smoke menthols. Numerous well-regarded reports, over time, confirm this conclusion. The magnitude and statistical strength of findings showing increased menthol use and menthol brand preference over time demonstrate that they are consistent and stable results from large representative national surveys and are unlikely to be due to chance, confounding, or bias.

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<sup>i</sup> We regard the term “relationship” as synonymous with the term “association.” See *Merriam-Webster Dictionary* (“association” defined as “1. a: the act of associating. b: the state of being associated : combination, relationship”), available at <http://www.merriam-webster.com/dictionary>. For clarity, we use the word “relationship” throughout these comments.

- **The prevalence of menthol cigarette use is higher in youth than young adults and adults.** The 2009 report from The National Survey on Drug Use and Health (NSDUH), *The NSDUH Report: Use of Menthol Cigarettes*, based on five years of survey data collection (2004, 2005, 2006, 2007, and 2008) with large representative sample sizes in the range of 70,000 annual interviews, provides an evidence-based estimate that in 2008, 44.7% of youth smokers (aged 12-17) smoked menthols. This compares with an overall menthol smoking rate (youth and adults) of 33.9%. From 2004 to 2008, menthol cigarette prevalence among youth ranged from 43.5% to 47.7%, among young adults (aged 18-25) from 34.1% to 40.8% and among adults (aged 26 and older) from 29.3% to 31.5%.<sup>5</sup> The stability of these nationally-representative estimates over five years highlights higher rates of menthol use in youth compared to adults from 2004 to 2008.
- **Menthol cigarette use is significantly higher in younger adolescents than older adolescents.** Estimates from the National Youth Tobacco Survey (NYTS), a survey administered to approximately 25,000 middle and high school students in each wave, demonstrate increased rates of menthol use among younger adolescent smokers. Results from the 1999, 2000, and 2002 surveys confirm a statistically significantly higher prevalence of menthol cigarette use among middle school students compared to high school students.<sup>6</sup> Published reports from more recent NYTS surveys in 2004, 2006, and 2009 have not addressed the prevalence of menthol cigarette use among youth and thus are not included in this submission.
- **Recent youth initiates are significantly more likely to use menthol cigarettes than youth who have smoked longer than one year.** Estimates from the NYTS and NSDUH also demonstrate increased menthol cigarette use among recent youth initiates. Two studies<sup>5,7</sup> combining waves of national data on youth smoking report a higher prevalence of menthol cigarette use among youth who have been smoking less than one year compared to those who have smoked more than one year. One of the studies combined data from five years of the NSDUH (2004-2008) and the other used two years of data from the NYTS (2000 and 2002). In the NSDUH study, past month smoking of menthol cigarettes was more likely among smokers aged 12 or older who began smoking in the past 12 months than among those who had been smoking for more than a year (44.6% vs. 31.8%). In the NYTS study, middle school students who had been smoking for less than one year were significantly more likely to smoke menthol cigarettes compared with middle school students who had been smoking for more than one year (62.4% vs. 53.3%,  $p = 0.002$ ).<sup>7</sup>
- **Menthol cigarette use among youth has significantly increased over the past decade.** Analyses in the NYTS<sup>7</sup> showed an 18.5% increase in overall youth menthol use from 2000 to 2002 (40.0% to 47.4%,  $p < 0.05$ ). This included a significant increase among middle school smokers (51.6% to 59.6%,  $p < 0.05$ ), but not among high school smokers (36.9% to 43.6%). Data from the NSDUH<sup>5</sup> show

an increase in menthol use of 9.7% from 2004 to 2008 (43.5% to 47.7%) among past month smokers aged 12-17. Reanalysis of overall trends in prevalence of smoking menthol and non-menthol cigarettes among adolescents (12-17 year olds) and young adults (18-25 year olds) from 2004-2008 using NSDUH data show that trends in use of menthol cigarettes among adolescents and young adults are either not changing or declining slightly. Among all youth and young adults, not just current smokers, the prevalence of smoking non-mentholated brands decreased more rapidly than the prevalence of smoking mentholated brands over this four-year period, indicating that menthol cigarettes are gaining market share in these age groups.<sup>9</sup>

- **Brand preference for menthol cigarettes has significantly increased among youth over time and especially among the youngest smokers (aged 13-14).** One study comparing three national surveys (The Robert Wood Johnson Foundation 1996 National Survey of Tobacco Price Sensitivity, Behavior, and Attitudes Among Teenagers and Young Adults and the TAPS-I and II surveys from 1989 and 1993) showed that brand preference for Newport, the most popular menthol brand among youth, increased significantly from 8.3% in 1989 to 12.5% in 1993 and 16.4% in 1996 ( $p < 0.01$ ) in adolescent smokers aged 13 to 18.<sup>8</sup> This study also reported that the percent of youth reporting usually buying Newport increased dramatically among the youngest smokers from 1989 to 1996: Over that time period there was a 347% increase among 13- to 14-year olds; a 189% increase among 15-year-olds; and a 69% increase among 16- to 18-year-olds. By way of comparison, youth preference for Marlboro and Camel cigarettes, the other two most popular brands among youth, remained unchanged across this time period. This study used large national samples of adolescents with approximately 9,000 respondents in 1989, 13,000 in 1993, and 17,000 in 1996 to demonstrate a statistically significant increase in youth menthol brand preference over a seven-year period. Further, the magnitude of the increase in brand preference for Newport cigarettes was most striking among the youngest smokers.
- **Young menthol smokers are more likely to switch to non-menthol cigarettes over time than the other way around,<sup>9</sup> underscoring menthol's role as a starter product.** Data from the National Youth Smoking Cessation Survey (NYSCS), a two-year (2003-2005) longitudinal telephone study of adolescent and young adult cigarette smokers aged 16-24 show that brand switching from menthol to non-menthol cigarettes is more prevalent than switching from non-menthol to menthol cigarettes. In this study of approximately 1,000 young smokers, 15.0% (95% CI: 10.8% - 19.2%) of baseline menthol smokers switched to non-menthol varieties after two years and 6.9% (95% CI: 4.9% - 8.9%) of baseline non-menthol smokers switched to mentholated cigarettes after two years. The differences in switching were especially noticeable for non-Hispanic whites and for those who were in college or had graduated from college at the time of the baseline survey. These data provide strong evidence that younger smokers are more likely to begin their smoking careers with mentholated products and progress to smoking non-mentholated varieties in a short period of time. This

lends further credence to evidence on menthol as a starter product for young smokers.

- **The findings regarding an age gradient in menthol cigarette use—increased levels of menthol smoking in the youngest age groups—are not attributable to menthol brand misclassification.** At the July 2010 TPSAC meeting, tobacco industry presentations criticized the classification of menthol smokers by the NSDUH survey. Re-analysis of the NSDUH data was conducted to address potential misclassification of menthol brand.<sup>ii</sup> The results of the re-analysis confirmed the earlier results, showing a statistically significant age gradient among 12-34 year olds, with the highest prevalence of menthol use among 12-17 year old smokers (49.3%, 95% CI: 47.8% – 50.7%), lower menthol use among 18-25 year old smokers (37.5%, 95% CI: 36.7% - 38.3%), and the lowest prevalence of menthol use among 26-34 year old smokers (29.9%, 95% CI: 28.5% - 31.3%). This age gradient persists for males, females, whites, blacks, Asians, and Hispanics. It is also present for those who smoke fewer than ten days per month and those who smoke ten days or more per month. Further examination of 12-25 year old smokers confirmed statistically significant differences in menthol use among the youngest smokers. Menthol use was highest among 12-15 year old smokers (53.5%), and decreased among 16-17 year old smokers (47.0%), 18-21 year old smokers (40.5%), and 22-25 year old smokers (34.6%). A statistically significant age gradient in these age categories was observed among males, females, and whites. These data bolster published results from the NSDUH survey showing that youth are more likely to smoke menthol than older adults and establish that these results are not an artifact of misclassification of menthol use.<sup>9</sup>
- **Industry insiders and experts have documented the appeal of menthol cigarettes as starter products.** Historical tobacco industry documents underscore menthol brands as starter products for youth (i.e., “Menthol brands have been said to be good starter products because new smokers appear to know that menthol covers up some of the tobacco taste and they already know what menthol tastes like, vis-à-vis candy”<sup>10</sup>) and recognize the importance of adolescent smokers to the success of menthol brands (i.e., “The success of Newport has been fantastic during the past few years. Our profile taken locally shows this brand being purchased by black people (all ages), young adults (usually college age), but the base of our business is the high school student”<sup>11</sup>). More recently, a tobacco industry expert at Morgan Stanley revealed that Newport is the choice of 17% of new smokers, even though the brand has only a 10% share of the market as a whole.<sup>12</sup>

In sum, ten years of national studies of tobacco use across different populations and time periods arrive at the same conclusions: there is a strong pattern of a higher—and growing—proportion of menthol cigarette use among youth (aged 12-17) than adults, and

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<sup>ii</sup> These results focus on exclusive menthol brands and thus, do not address possible misclassification of Marlboro Menthol or other non-exclusive menthol brands.

especially among younger adolescents and recent youth initiates. The results from large, representative studies provide evidence of a relationship between menthol and youth smoking that is robust and consistent in magnitude and direction and is unlikely to be due to bias, confounding or chance.

More particularly, the replication of these findings over time using different studies and populations provides evidence of consistency. The increasing prevalence of youth menthol use and brand preference across the years of the NSDUH, NYTS, TAPS, and Robert Wood Johnson Foundation studies underscores the strength of the association between menthol and youth smoking. Data showing a high prevalence of menthol use among youth, in addition to higher prevalence among younger adolescents and recent initiates, and increasing menthol use over time, supports coherence of the evidence on menthol and youth smoking. Plausibility of the relationship between menthol and youth smoking is corroborated by historic industry and related documents on the development and marketing of mentholated cigarettes to youth.<sup>10,11</sup> The magnitude and statistical significance of the data on the increasing proportion of menthol use and brand preference among youth over time reveals that this is a national phenomenon.

The statistically significant 17% difference in menthol use among middle school students compared to high school students demonstrates that the association between menthol use and recency of smoking initiation among youth is unlikely to be due to chance or confounding. Additional analyses presented by Dr. Gary Giovino at the November 18, 2010 TPSAC meeting also exclude misclassification as an explanation for the strong relationship between menthol use and youth initiation and provide evidence for the progression of young smokers from mentholated to non-mentholated cigarettes over a short time period.

While the cross-sectional nature of the national surveys precludes a determination as to whether there is a temporal relationship between menthol and youth initiation—a finding not necessary, in any event, to establish a relationship—evidence from the longitudinal NYSCS demonstrates a temporal relationship in progression from menthol to non-menthol cigarettes among young smokers by indicating that young smokers are more likely to switch from menthol to non-menthol cigarettes over a two-year period.

Thus, after a careful review of the body of evidence, we conclude that there is sufficient evidence of a relationship between menthol and increased youth smoking initiation, or, otherwise stated, the existence of a relationship between menthol and youth smoking initiation is more likely than not.

Given the strong and established pattern of menthol use by the youngest and newest smokers, it is more likely than not that a ban on menthol will result in lower rates of youth smoking initiation. There is no experiment that can be undertaken in advance of an actual ban to test or otherwise indicate what proportion of youth and young adults would be prevented from smoking as a result of a ban. However, these data persuasively suggest that fewer youth will start to smoke if menthol products are not available to them. As discussed in greater detail in the section below on risks and benefits, even a small

percentage reduction in youth initiation would result in a cumulative and very significant public health benefit, given the overwhelming harms caused by cigarette smoking.

### **The Scientific Evidence on Menthol and Adult Smoking Cessation Demonstrates a Likelihood That a Ban on Menthol Will Result in Higher Rates of Smoking Cessation**

The weight of the scientific evidence shows that adult menthol smokers are less likely than adult non-menthol smokers to successfully quit smoking despite increased quit intentions and quit attempts.<sup>iii</sup> While these results apply across most population groups, we note in particular, and consistent with Congress' explicit direction to TPSAC, that minority menthol smokers are notably less likely to successfully quit than minority non-menthol smokers.

- **Three studies in the TUS-CPS** measure both quit attempts or intention to quit and cessation outcomes. Of these, two<sup>13,14</sup> demonstrate that menthol users are less successful in quitting than non-menthol users despite increased quit attempts or intentions to quit. The third study<sup>15</sup> found no difference between menthol and non-menthol smokers. For the reasons discussed below, the third study should be given less weight than the first two.
  - In a study of cessation by racial/ethnic groups,<sup>13</sup> African American and Hispanic/Latino menthol smokers had significantly increased intention to quit and positive estimation of quit success compared to African American and Hispanic/Latino non-menthol smokers, controlling for age, gender, education, daily/non-daily smoking, smoking within 30 minutes of waking, current use of other tobacco products, and interest in quitting smoking. In contrast, cessation of at least six months was significantly reduced by 52% to 78% in African American, Hispanic/Latino, Asian American/Pacific Islander, and non-Hispanic white menthol smokers compared to non-menthol smokers controlling for age, education, gender and current use of other tobacco products; cessation was reduced, but not statistically significantly, among Native American/Alaska Native menthol smokers.
  - A second study<sup>14</sup> of 65,510 adults found that past-year quit attempts were significantly increased in menthol compared to non-menthol smokers, but quit rates were significantly lower among those who smoke menthol cigarettes as compared to non-menthol cigarettes, controlling for demographics, state-level tobacco control policies, and nicotine dependence. The likelihood of quitting

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<sup>iii</sup> Other studies look solely at whether menthol smokers are more likely to make quit attempts than non-menthol smokers. *See, e.g.,* Alexander LA, Crawford T, Mendiondo MS. Occupational status, worksite cessation programs and policies, and menthol smoking on quitting behaviors of US smokers. *Addiction*. Dec 2007;102(12):95-104; Fagan P, Augustson E, Backinger CL, et al. Quit attempts and intention to quit cigarette smoking among young adults in the United States. *Am J Public Health*. Aug 2007;97(8):1412-1420. Because our interest is in the effect of menthol cigarette use on smoking cessation, we focused on studies that used cessation measures in addition to measures of quit attempts or intention to quit.

was about 3.5% lower for those quit in the last year and about 6% lower for those who quit within the last 5 years. This study also showed a significant decrease in longer-term cessation among African American menthol smokers and young adult (18-24) menthol smokers compared to non-menthol smokers.<sup>14</sup>

- The third study<sup>15</sup> examined quitting behaviors among daily menthol and non-menthol smokers with similar cigarette consumption patterns and found no difference in quit attempts or greater than two-week abstinence by menthol status, after controlling for demographic characteristics which were modeled differently for each level of consumption (i.e., 1-5 cigarettes per day, 6-10 cigarettes per day, 11-19 cigarettes per day, and 20+ cigarettes per day). Specifically, gender and race/ethnicity were not included in all models.
- The size and representative nature of the large, national TUS-CPS survey provides robust evidence for reduced cessation among adult menthol smokers in the United States. The first two TUS-CPS studies, both of which demonstrated consistent, strong relationships between menthol use and decreased long-term cessation, analyzed data from current and former smokers and consistently controlled for important confounders. They highlighted the discrepancy between quit attempts or intention to quit and quit success in menthol smokers. The third study, which did not show a difference in quitting behaviors by menthol status, used data from daily smoking adults which may be a more selected population than current and former smokers, did not consistently control for gender and race/ethnicity, and used a short-term cessation measure of two-week abstinence as compared to the much longer and more reliable measures in the other two studies. For these reasons, this study should be given less weight in the overall synthesis of the TUS-CPS data.
- **Studies of adult smokers in the 2005 National Health Interview Survey Cancer Control Supplement** corroborate the findings for reduced cessation among racial and ethnic subgroups from the TUS-CPS data. These studies report increased quit attempts in the past year among menthol compared to non-menthol smokers<sup>16,17</sup> but significantly reduced cessation among African-American<sup>16,18</sup> and Hispanic menthol smokers compared to non-menthol smokers.<sup>18</sup> One of these studies<sup>18</sup> also collapsed Hispanic and African-American smokers into one category and reported a statistically significant decrease of 45% in the odds of cessation among non-white menthol smokers compared to non-white non-menthol smokers. The single study assessing quit duration as a cessation measure showed that there was a significant increase in length of quit among white female menthol smokers compared to white female non-menthol smokers, but no statistically significant differences among the other five demographic groups.<sup>17</sup> Similar to the studies in the TUS-CPS, two of these three NHIS studies<sup>16,18</sup> assessing cessation beyond quit attempts also controlled for demographic and smoking variables considered to be potential confounders. Results from these two studies add to the consistency of findings from nationally-

representative surveys on reduced cessation among racial/ethnic subgroups of menthol smokers and further support the strength of the association between menthol use and reduced adult cessation.

- **Cohort studies and randomized controlled trials** exploring menthol's effect on smoking cessation also point to reduced cessation rates among menthol compared to non-menthol smokers.
  - Of three cohort studies examining differences in smoking cessation,<sup>19,20,21</sup> two report significantly lower quit rates among menthol smokers compared to non-menthol smokers at follow-up.<sup>20,21</sup> One<sup>20</sup> of these two cohort studies showed a 37% reduction in the odds of sustained cessation adjusted for age, sex, and ethnicity, but this result did not retain statistical significance after additional adjustment for educational level, marital status, employment, and health insurance status. The other of the two<sup>21</sup> reports significant reductions in the odds of cessation of 68% and 57% among African American and Latino menthol smokers, respectively, at 4-week follow-up and a decrease of 52% in African Americans at 6-month follow-up, controlling for age in years, education, gender, employment status, type of insurance, cigarettes per day, age smoked for first time, awoken at night to smoke, time to use first cigarette of day, previous attempts to quit smoking, and the presence of a disease caused or aggravated by smoking. The COMMIT study,<sup>19</sup> which did not show a difference in cessation between menthol and non-menthol smokers, surveyed smokers in selected communities in the U.S. and Canada between 1988 and 1993. Possible reasons for the mixed results across the three studies include population sampling and recency of the data. Of the two studies showing a statistically significant difference in cessation by menthol smoking status, one<sup>21</sup> was conducted in a cessation clinic population from 2001 to 2005 and the other<sup>20</sup> in a large cohort of healthy young African American and European American men and women in four US cities from 1985 through 2000. We would note that the cigarette market has undergone dramatic changes over the past 10-15 years, including the introduction of a number of new menthol brands.<sup>22</sup> Because of the differences in menthol levels and effects among brands,<sup>23</sup> it is important to rely on the most recent data that reflects products currently on the market. Accordingly, we consider the latter two studies more relevant to the question of adult cessation in the context of an FDA ban on menthol, as they include more recent data. Additional weight should also be given to the cohort study conducted in a cessation clinic, as it reflects smokers who are motivated to quit and thus, controls for confounding by cessation cognitions and intention to quit.
  - Three randomized controlled trials<sup>24,25,26</sup> in clinical populations motivated to quit smoking also explored the impact of menthol cigarette use on cessation. One study testing the impact of a phone survey and provider progress notes on smoking cessation among VA patients showed no difference six months after the intervention in smokers who had not smoked in the past seven days.<sup>24</sup>

However, two studies<sup>25,26</sup> testing the effect of pharmacotherapies and behavioral therapies on smoking cessation reported significantly reduced cessation among African American menthol smokers. While results in these two studies maintained a consistent direction (i.e., menthol users had reduced cessation compared to non-menthol users), they were not statistically significant across all follow-up time points. One major difference in these studies is focus of the cessation intervention. The two studies<sup>25,26</sup> testing the impact of an individual-level intervention showed reduced cessation among menthol smoking participants while the provider-focused intervention<sup>24</sup> showed no difference in cessation among menthol and non-menthol smoking participants. The studies focusing on individual-level interventions are more relevant to the question of menthol's influence on smoking cessation, as they capture a seven-to-eight week window of evidence-based treatment for smoking cessation rather than a single provider visit.

- Of the three cohort studies and three randomized controlled trials (six studies in all), four are consistent in reporting reduced cessation at follow-up among menthol compared to non-menthol smokers.<sup>20,21,25,26</sup> Evidence from these four studies with consistent results also support the temporal relationship between menthol smoking and reduced smoking cessation through their study designs which included longitudinal follow-up of adult smokers.

Two of three studies in the TUS-CPS<sup>13,14</sup> and two of three studies in the Cancer Control Supplement to the National Health Interview Survey<sup>16,18</sup> that examined quit attempts and additional cessation measures among adult smokers indicate that cessation is reduced in non-Hispanic whites and in racial and ethnic subgroups of menthol smokers compared to non-menthol smokers despite increased quit attempts. These findings demonstrate reasonable consistency and a coherent picture of quit behavior among menthol smokers: menthol smokers make more quit attempts than non-menthol smokers, yet have a more difficult time quitting successfully. Two<sup>20,21</sup> of three cohort studies and two<sup>25,26</sup> of three randomized controlled trials contribute to the consistency of the findings and the strength of the association between menthol smoking and reduced cessation among adult smokers. In addition, these four studies also demonstrate that menthol smoking precedes reduced cessation, as they measure cessation success at follow-up. Further, these findings are plausible in light of historic tobacco industry marketing of menthol cigarettes as medicinal, less harmful, or even a more healthful product than non-menthol cigarettes<sup>27,28,29,30</sup> and the resulting perceptions among menthol smokers that menthol cigarettes may be less risky than regular cigarettes.<sup>31</sup> The above-referenced cross-sectional,<sup>13,14,16,18</sup> cohort<sup>21</sup> and randomized controlled studies,<sup>25,26</sup> which showed strong and consistent relationships between menthol use and reduced smoking cessation, were high quality, and addressed bias and confounding through regression adjustment or randomization. While there is some inconsistency of findings across all studies, taken as a whole, these studies establish that the existence of a relationship between menthol smoking and reduced cessation is more likely than not under the classification scheme recommended by TPSAC.

The strength and consistency of the relationships shown in these data persuasively suggest that the removal of menthol from cigarettes would more likely than not improve smoking cessation outcomes. As with youth initiation, it is not possible to approach the question experimentally to determine what proportion of current menthol smokers would be able to quit smoking successfully as a result of a ban. However, as explained in more detail below, due to the tremendous harms of smoking, even small reductions in adult smoking prevalence would have important population-level effects on smoking-related morbidity, mortality, and medical costs, as well as reductions in youth smoking prevalence via changes in the social environment.<sup>32,33</sup>

### **The Scientific Evidence Demonstrates that the Benefits of a Menthol Ban Far Outweigh the Risks**

*Risks and Benefits to Non-Smokers, Primarily Youth.* A menthol ban poses *no risks at all* to non-smokers, most importantly to the young teenagers to whom menthol is so attractive. There are only benefits. The great harms associated with smoking initiation among youth are well-established and widely accepted.<sup>34</sup> Results from the 50-year follow-up to the British Doctors' Study demonstrate the importance of quitting smoking before age 30 to avoid tobacco-related mortality.<sup>35</sup> It is no longer disputed that cigarette smoking causes cancer, heart disease, respiratory disease, low birth weight, sudden infant death syndrome, and other serious health effects. It is similarly beyond dispute that even modest reductions in tobacco initiation among youth would result in significant reductions in premature tobacco-related death on a population level.<sup>36</sup>

*Risks and Benefits to Current Smokers.* Addicted menthol smokers who choose to quit smoking in the face of a menthol ban may encounter temporary withdrawal symptoms that would be encountered by any addicted smoker who stops smoking. There is no scientific evidence, however, linking smoking cessation to any serious physical health risks. There is some evidence that smoking cessation can exacerbate certain mental health problems in smokers who suffer from such problems,<sup>37</sup> but there is no evidence that these risks are either large or widespread. We do not minimize the very real difficulties encountered by addicted smokers in successfully quitting. We are mindful of the research discussed above which demonstrates that menthol smokers have lower success rates than non-menthol smokers in quitting. However, the risks of withdrawal symptoms are manageable through well-established, evidence-based treatments. Of particular importance, these risks pale in comparison to the indisputable and very significant benefits of quitting. This is certainly true for the African-American and other minority menthol smokers who the evidence shows are particularly less likely to quit and whom the FDA is specifically instructed to take into account in connection with its consideration of a menthol ban. Even a modest increase in cessation rates following a menthol ban would result in significant benefits to the public health on a population basis. Of course, since what is at issue is a ban on menthol and not a ban on all cigarettes and other tobacco products, addicted smokers could certainly choose to avoid withdrawal symptoms altogether by switching to unflavored cigarettes, smokeless tobacco, or cigars.

In evaluating the risks of a menthol ban, we would note that Congress was principally concerned with the “sudden” or “precipitous” removal of menthol products from the market.<sup>38</sup> Accordingly, and consistent with broader principles of public health, we encourage TPSAC to recommend that the FDA provide prior notice of a menthol ban. It should use the time period between the notice and the actual implementation of the ban to provide public education on the benefits and possible methods of quitting and also to support the availability of evidence-based cessation services and treatments.

*Estimation of the impact of a menthol ban on smoking prevalence.* Using data from the 2007 NSDUH, we estimate that there are nearly 60 million past-month smokers in the United States. Of these, approximately two million are aged 12-17, 12 million are aged 18-25 and 46 million are aged 26 and older. Given the prevalence of menthol smoking in these age groups, we estimate that there are 20 million past-month menthol smokers in the United States. As presented in the table below, changes in smoking prevalence pursuant to a ban on menthol in cigarettes could have dramatic population-level effects. Even an exceedingly conservative estimate of a 0.1% reduction in smoking prevalence among menthol smokers would mean approximately 1,000 fewer youth smokers, 4,500 fewer young adult smokers, and 14,000 fewer smokers over the age of 26—a total of more than 19,000 smoking careers either shortened or entirely averted. With larger—but still modest—estimated effects of the ban on menthol smoking prevalence, the effect is magnified demonstrating tremendous public health benefit. Given that half of all lifetime smokers die prematurely from a smoking-attributable illness,<sup>39</sup> any one of these estimates will translate into thousands of premature deaths averted.

<b>Reduction in past-month smoking prevalence (Number of past-month menthol smokers)</b>							
	<b>Percent menthol smokers</b>	<b>Baseline</b>	<b>0.10%</b>	<b>1%</b>	<b>5%</b>	<b>10%</b>	<b>15%</b>
<b>Menthol ban</b>							
<b>Youth</b>							
12-17	47.7%	1,048,653	(1,049)	(10,487)	(52,433)	(104,865)	(157,298)
<b>Adults</b>							
18-25	38.5%	4,561,859	(4,562)	(45,619)	(228,093)	(456,186)	(684,279)
26 or older	30.4%	13,910,782	(13,911)	(139,108)	(695,539)	(1,391,078)	(2,086,617)
<b>Net reduction in number of smokers</b>		-	(19,521)	(195,213)	(976,065)	(1,952,129)	(2,928,194)

## **Risks of a Black Market in Menthol Cigarettes**

Opponents of a menthol ban vigorously argue that a ban will result in a black market of unregulated and possibly counterfeit menthol cigarettes. They suggest that these cigarettes will be more dangerous than cigarettes currently on the market. Given the exceedingly limited nature of the scientific evidence, it may be that this is not an appropriate subject for TPSAC to address. Insofar as TPSAC does offer advice to FDA on the black market set of issues, we suggest that it take into account the following points.

First, in evaluating claims regarding relative harms of legal and contraband cigarettes, legally-available menthol cigarettes, like all cigarettes, are already exceedingly dangerous, killing roughly half of lifelong users. The mere fact that contraband cigarettes would be very dangerous—which is undoubtedly true—simply reflects the essential nature of this lethal product.

Second, with regard to the extent of a potential black market, while a menthol ban may lead to some level of illegal sales, the vast majority of menthol smokers are likely to comply with the law. As has been observed in other contexts, the use of illegal drugs carries a high cost for the user, including fear of apprehension, punishment, and cost in time and worry in acquiring an illegal substance.<sup>40</sup> In addition, it is important to keep in mind that what is under consideration is a ban on menthol products—not a ban on all cigarettes. As discussed above in connection with the potential risks of a menthol ban, menthol smokers who are not able to, or choose not to, quit will have full legal access to unflavored cigarettes and other tobacco products as well as a myriad of approved cessation assistance medications.

Third, the recently-enacted PACT Act provides strong disincentives to the illegal smuggling of tobacco products, which will also help deter those tempted to buy or sell menthols illegally.<sup>41</sup> TPSAC should recommend that a menthol ban be accompanied by additional enforcement measures, including stiff penalties for smugglers and stringent record-keeping requirements for manufacturers and importers, to prevent a significant black market from developing. Other federal agencies considering limiting or banning particular products or substances have determined that similar measures made a significant black market unlikely.<sup>42</sup> For example, in announcing its intent to impose limits on the use of the pesticide methyl bromide, the EPA noted that the existing controls on the shipment, sale, and use of the pesticides, as well as stringent penalties for violating Clean Air Act record-keeping requirements, made the development of a black market for the substance unlikely.<sup>43</sup> In another context, the Department of Agriculture considered a number of factors in concluding that the imposition of a tariff was unlikely to give rise to a black market for avocados, including the fact that “persons involved in such illegal transshipment are liable to legal action, incarceration, or fines.”<sup>44</sup>

Finally, the very cigarette companies that raise the specter of a large black market will play a significant role in determining whether or not such a black market arises. Studies on cigarette smuggling in other countries indicate the strong role of the tobacco industry itself in the facilitation of these illegal activities.<sup>45</sup> In addition, the fact that the top

menthol brand is exclusively manufactured in the United States<sup>46</sup> strongly suggests that its manufacturer, Lorillard Tobacco Company, could exercise a great deal of control over any smuggling of its legitimate products and should partner with the FDA in efforts to combat a possible black market.

In sum, there is no scientific support for the proposition that a large black market of more dangerous counterfeit or contraband menthol cigarettes will arise. Moreover, the law enforcement tools currently in place along with reasonable enhancements will be well-suited to address the black market and related issues that may arise.

## CONCLUSION

For the reasons set forth above, a review of the scientific evidence demonstrates that there is sufficient evidence to establish a relationship between menthol and (1) increased youth smoking initiation and (2) decreased adult cessation. As a consequence, a menthol ban is more likely than not to result in decreased youth initiation and increased adult cessation. Moreover, the likely benefits of a menthol ban of decreased youth initiation and increased adult cessation will substantially outweigh the risks of such a ban. These risks, which only affect addicted smokers, are manageable by providing adequate advance notice of a ban and assuring the provision of cessation services and treatments. There are no risks at all of a menthol ban to non-smokers, most importantly, youth. Finally, there is, at most, scant scientific evidence to support the concerns which have been raised regarding the creation of a black market and dangers caused by counterfeit or contraband menthol cigarettes. We have presented other evidence that supports the view that the problems will not be nearly as severe as some would suggest. To the extent these problems may arise, they are properly managed through law enforcement tools and tobacco industry cooperation.

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<sup>1</sup> H.R. Rep. No. 111-58, at 39 (2009).

<sup>2</sup> Food, Drug, and Cosmetic Act ("FDCA"), as amended by the Family Smoking Prevention and Tobacco Control Act ("Tobacco Control Act"), § 907(a)(3)(B)(i).

<sup>3</sup> See, e.g., Tobacco Control Act § 2 ("The use of tobacco products by the Nation's children is a pediatric disease of considerable proportions that results in new generations of tobacco-dependent children and adults.")

<sup>4</sup> See, e.g., *United States v. Article of Drug... Bacto-Unidisk*, 394 U.S. 784, 798 (1969) (The Food, Drug & Cosmetic Act is "to be give a liberal construction consistent with [its] overriding purpose to protect the public health.").

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## APPENDIX A

### Studies used to assess role of menthol in smoking initiation and cessation

#### *National surveys*

Data from the following five surveys provide information on the national prevalence of menthol cigarette use among youth and adults. All of these studies are conducted with the highest scientific and professional standards under the purview of U.S. government agencies, including the Centers for Disease Control and Prevention (CDC), the Substance Abuse and Mental Health Services Administration (SAMHSA), and the National Cancer Institute (NCI). In addition, experts in the field and leading non-governmental research companies (i.e., Macro International Inc., Westat Inc., and Research Triangle Institute) have developed the methods and questionnaires for these studies to generate estimates from the data that reflect patterns in the broader U.S. population.

#### National Survey on Drug Use and Health (NSDUH)

The National Survey on Drug Use and Health (NSDUH) is an annual nationwide survey involving interviews with approximately 70,000 randomly selected individuals aged 12 and older. The Substance Abuse and Mental Health Services Administration (SAMHSA), which funds NSDUH, is an agency of the U.S. Public Health Service in the U.S. Department of Health and Human Services (HHS). Since 1988, Research Triangle Institute (RTI) has been selected to conduct the survey through a competitive bidding process; supervision of the project comes from SAMHSA's Office of Applied Studies (OAS). RTI's role in this long-term national effort includes study design, sample selection, data collection, data processing, analysis, and reporting. Data from the NSDUH provide national and state-level estimates on the use of tobacco products, alcohol, illicit drugs (including non-medical use of prescription drugs) and mental health in the United States. In keeping with past studies, these data continue to provide the drug prevention, treatment, and research communities with current, relevant information on the status of the nation's drug usage. For more information on this survey, visit <https://nsduhweb.rti.org/>.

#### National Youth Tobacco Survey (NYTS)

In collaboration with CDC, the American Legacy Foundation developed the National Youth Tobacco Survey to measure the tobacco-related beliefs, attitudes and behavior of youth, and the pro- and anti-tobacco influences to which they are exposed. The NYTS was designed to estimate tobacco use, attitudes towards tobacco use, cessation attempts, exposure to second-hand smoke, and environmental factors in a national population of students in grades 6 through 12. It provides national data on long-term, intermediate, and short-term indicators key to the design, implementation, and evaluation of comprehensive tobacco prevention and control programs and serves as a baseline for comparing progress toward meeting selected Healthy People 2010 goals for reducing tobacco use among youth. NYTS data collection and methods allow researchers to produce national estimates of these characteristics as measured by the NYTS questionnaire by school grade level (middle, high), by specific grade (6, 7, 8, 9, 10, 11, 12), by gender, and by race/ethnicity (African American, Hispanic, and Asian). The first NYTS was conducted in 1999, with subsequent surveys in 2000, 2002,

2004, 2006, and 2009. Sample sizes across these years range from approximately 15,000 to 36,000 respondents. For more information on this survey, visit [http://www.cdc.gov/tobacco/data\\_statistics/surveys/nyts/index.htm](http://www.cdc.gov/tobacco/data_statistics/surveys/nyts/index.htm).

#### National Health and Nutrition Examination Surveys (NHANES)

The National Health and Nutrition Examination Survey (NHANES) is a program of studies designed to assess the health and nutritional status of adults and children in the United States. The survey is unique in that it combines interviews and physical examinations and is conducted regularly in two-year intervals. NHANES is a major program of the National Center for Health Statistics (NCHS). NCHS is part of CDC and has the responsibility for producing vital and health statistics for the Nation. Approximately 5,000 people are surveyed each year; the sample for the survey is selected to represent the U.S. population of all ages. To produce reliable statistics, NHANES over-samples persons 60 and older, African Americans, and Hispanics. For more information on this survey, visit [http://www.cdc.gov/nchs/nhanes/about\\_nhanes.htm](http://www.cdc.gov/nchs/nhanes/about_nhanes.htm).

#### Teenage Attitudes and Practices Survey (TAPS)

The Teenage Attitudes and Practices Survey (TAPS) was a follow-up study to the National Health Interview Survey (NHIS), the principal source of information on the health of the civilian non-institutionalized population of the United States. The first TAPS (TAPS-I) was conducted in 1989 and the second TAPS (TAPS-II) was conducted in 1993. The TAPS-II sample had two components. The first TAPS-II sample component is a follow-up of the TAPS-I telephone sample and was comprised of persons aged 12-18 years on November 1, 1989. Respondents for TAPS-II included the 9,135 teenagers who responded by telephone to TAPS-I (aged 15-22 years at the time of TAPS-II), and 5,590 new adolescents aged 10-15 years who were drawn from quarters three and four of the 1991 NHIS and quarter one of the 1992 NHIS sample frames. The TAPS provides national estimates of adolescent tobacco use in 1989 and 1993, in addition to providing data at both time points for more than 9,000 adolescents. For more information on the TAPS, visit [http://wonder.cdc.gov/wonder/sci\\_data/surveys/nhis/type\\_txt/tapsii.asp](http://wonder.cdc.gov/wonder/sci_data/surveys/nhis/type_txt/tapsii.asp).

#### National Youth Smoking Cessation Survey (NYSCS)

The National Youth Smoking Cessation Survey (NYSCS) was a two-year (2003-2005) longitudinal telephone study of adolescent and young adult cigarette smokers aged 16-24. Funded by Robert Wood Johnson Foundation, CDC, and NCI, this national study helped to fill a critical gap in knowledge by providing insight into adolescent and young adult quitting behavior; tracking changes in quitting behavior over time; and clarifying preferences for different types of assisted quitting interventions. The NYSCS is the only national survey with a representative cohort of older youth and young adult smokers. For more information on the NYSCS, visit [http://www.rwjf.org/files/research/NYSC%20Summary\\_RWJFfinal.pdf](http://www.rwjf.org/files/research/NYSC%20Summary_RWJFfinal.pdf).

#### Tobacco Use Supplement to the Current Population Survey (TUS-CPS)

The Tobacco Use Supplement to the Current Population Survey (TUS-CPS) is an NCI-sponsored survey of tobacco use that has been administered as part of the U.S. Census Bureau's Current Population Survey in 1992-1993, 1995-1996, 1998-1999, 2000, 2001-2002,

2003, and 2006-2007. The CDC has been a co-sponsor with NCI since 2001-02. The TUS-CPS is a key source of national and state level data on smoking and other tobacco use in the U.S. household population because it uses a large, nationally representative sample that contains information on about 240,000 individuals within a given survey period. For more information on the TUS-CPS, visit <http://riskfactor.cancer.gov/studies/tus-cps/>.

#### National Health Interview Survey Cancer Control Supplement

The National Health Interview Survey (NHIS) is a continuing, nationwide, in-person survey of approximately 40,000 households, or about 100,000 persons, in the civilian non-institutionalized population. The NHIS serves as the main source of data on health. It has historically been used for monitoring health patterns and trends and tracking progress towards national goals. Data from NHIS also are widely used for research and policy analyses. NCI periodically sponsors a Cancer Control Supplement (CCS) that is administered to a randomly selected sample of 39,000 adults. The CCS was first administered in 1987 to one sample adult aged 18 years or older in each household that participated in the NHIS. The CCS was subsequently administered in 1992, 2000, 2005, and 2010. A subset of cancer screening questions has been administered intermittently since 2000. For more information on the CCS, visit: <http://appliedresearch.cancer.gov/surveys/nhis/what.html>

#### *Cohort studies*

Gandhi K, Foulds J, Steinberg M, Lu S, Williams J. Lower quit rates among African American and Latino menthol cigarette smokers at a tobacco treatment clinic. *Int J Clin Pract.* Mar 2009;63(3):360-367.

This is a retrospective cohort analysis of 1688 consecutive patients who set a quit date and attempted to quit smoking, between 1 January 2001 and 30 June 2005. They all attended a specialist tobacco dependence treatment outpatient clinic in New Jersey. This clinic provides multidisciplinary treatment to a diverse population of tobacco users. The study population included 778 menthol cigarette smokers and 910 non-menthol cigarette smokers.

Hyland A, Garten S, Giovino G, Cummings K. Mentholated cigarettes and smoking cessation: findings from COMMIT. Community Intervention Trial for Smoking Cessation. *Tob Control.* Jun 2002;11(2):135-139.

COMMIT was a randomized community based intervention trial for smoking cessation in 11 matched pairs of communities—10 pairs in the USA and one pair in Canada. The COMMIT cohort was identified by a telephone survey in 1988. Subjects included in this analysis were smokers between 25–64 years of age at baseline who reported whether their current cigarette brand was mentholated or not in 1988, and had a known smoking status in 1993. A total of 13,268 cohort members met these criteria out of the 20,347 subjects who originally participated in the COMMIT cohort in 1988.

Pletcher M, Hulley B, Houston T, Kiefe C, Benowitz N, Sidney S. Menthol cigarettes, smoking cessation, atherosclerosis, and pulmonary function: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Arch Intern Med.* Sep 2006;166(17):1915-1922.

The Coronary Artery Risk Development in Young Adults (CARDIA) Study has collected detailed longitudinal data on smoking habits during 15 years of follow-up in a large cohort of 5,115 African American and European American women and men aged 18 to 30 years and healthy at the time of enrollment in 1985 in four U.S. cities. For this investigation, the authors identified CARDIA smokers and measured relationships between menthol/non-menthol exposure and smoking cessation behaviors during follow-up, the prevalence of coronary calcification in 2000, and changes in pulmonary function test results between 1985 and 1995.

### *Randomized controlled trials*

Fu S, Okuyemi K, Partin M, et al. Menthol cigarettes and smoking cessation during an aided quit attempt. *Nicotine Tob Res.* Mar 2008;10(3):457-462.

This is a secondary analysis of data from a multi-site randomized controlled trial of an intervention to facilitate repeat tobacco cessation treatment. Participants were identified from the Department of Veterans Affairs (VA) pharmacy databases and included smokers with a recent quit attempt that incorporated pharmacologic treatment. 1,900 subjects age 19 or older who had received a prescription for nicotine replacement therapy (NRT) or bupropion for smoking cessation between February and October 2002 from one of five participating VA medical centers were randomly assigned to either the intervention or usual care. The study population included 342 menthol smokers and 1,001 non-menthol smokers.

Okuyemi K, Ahluwalia J, Ebersole-Robinson M, Catley D, Mayo M, Resnicow K. Does menthol attenuate the effect of bupropion among African American smokers? *Addiction.* Oct 2003;98(10):1387-1393.

The parent study was a double-blind, placebo-controlled, randomized trial of 600 African American smokers conducted from 1999 to 2000.<sup>1</sup> Participants were recruited at an inner-city community health center over a 16-month period and were assigned randomly to receive a 7-week supply of placebo or bupropion SR 150 twice daily. The study population included 471 menthol smokers and 129 non-menthol smokers.

Okuyemi K, Faseru B, Sanderson Cox L, Bronars C, Ahluwalia J. Relationship between menthol cigarettes and smoking cessation among African American light smokers. *Addiction.* Dec 2007;102(12):1979-1986.

The primary study was a double-blind, placebo-controlled, randomized trial of African American light smokers conducted from 2003 to 2004 at a community-based health center serving a predominately African American population. This is a secondary analysis of data from a study that assessed the efficacy of 2 mg nicotine gum and counseling for smoking cessation among African American light smokers (smoked  $\leq 10$  cigarettes per day). The study population included 615 menthol smokers and 140 non-menthol smokers.

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<sup>1</sup> Ahluwalia JS, Harris KJ, Catley D, Okuyemi KS, Mayo MS. Sustained-release bupropion for smoking cessation in African Americans: a randomized controlled trial. *JAMA.* Jul 24-31 2002;288(4):468-474.